REMARKS

I. Claims in the Case

Claims 1-3, 26-28 and 35-37 have been cancelled. Claims 4-10, 12-19, 22, 23, 25, 29 and 31–32 have been amended. Claims 11, 13-18, 20, 21 and 24 are withdrawn. Claims 38-45 have been added. Claims 4-10, 12, 19, 22-23, 25 and 29-34 and 38-45 are currently pending and under examination.

The claims have been amended to focus the present prosecution on transduced hematopoeitic cells, and thus claim 29 has been placed into independent form. It is noted for the record that the lentiviral transfer "vector" of claim 1 is actually used in the preparation of the recombinant SIN lentivirus (in a producer host cell) that is subsequently used to transduce target cells such as hematopoietic progenitor cells. It is noted that claim 29 has been expanded to include hematopoietic cells in general, and the promoter aspect has been amended to clarify that the promoter is one that is active in either progenitor or differentiated hematopoietic cells. Support for these amendments can be found in the specification at various places, including particularly page 17, lines 25-29 (promoters); Example 3, which begins at page 57 (erythroid cells, granulocytes, monocytes, dendritic cells) and Example 4, which begins on page 58 (B cells, T lymphocytes).

Further, for the record, previously pending claim 1 had a slight error in it. The packaging genes *gag*, *pol* and *rev* are, for safety reasons, preferably contained on a separate "packaging plasmid" that is distinct from the recombinant transfer lentivector which carries the desired recombinant gene. See, for example, US 5,994,136 and Zufferey *et al.*, incorporated into the present application at page 26, lines, 6-7. This is no longer an issue since none of the currently pending claims now requires the inclusion of the packaging genes *gag*, *pol* and *rev*.

New claims 38-45 have been added to specify particular hematopoietic cells. Support for this amendment can be found, for example, in Examples 3 and 4 as noted above.

II. Double Patenting

The Action first provisionally rejects various of the claims over various claims of later-filed copending application 10/261,078. In response to this rejection, Applicants note that the '078 application is still pending and no claims have been allowed. Furthermore, the pending claims relied upon by the present Action have been cancelled and new claims added in (a copy of which is enclosed). It is submitted that the present claims are patentably distinct from the currently pending claims in the '078 case.

III. Anticipation Rejection over Ramezani *et al.*

The Action next rejects claims 1-10, 19, 22-23, 25-36 as anticipated by Ramezani *et al.*

In response, Applicants first note that Ramezani *et al.* was published in November of 2000, and thus is available as prior art only under 35 U.S.C. §102(a). However, the present inventors made the present invention well prior to November 2000, as evidenced by the enclosed Salmon *et al.* article, which was submitted for publication in February of 2000. The enclosed Rule 131 declaration of the inventors is submitted to demonstrate that the present invention, at least so much as is disclosed by Ramezani *et al.*, was made prior to date that the Ramezani *et al.* article was published.

It is submitted that the enclosed declaration adequately demonstrates that the Ramezani *et al.* publication is not prior art under 35 U.S.C. §102(a).

IV. Anticipation Rejection Over Zufferey *et al.*

The Action next rejects claims 1-5 as anticipated by Zufferey *et al.*, with the Action taking the position that Zufferey *et al.* discloses SIN vectors employing a CMV promoter and that CMV promoters are known to be able to at least promote detectable expression in hematopoietic cells.

In response, it is noted that this rejection is now moot in light of the fact that claim 29 was not included in the rejection and pending claims 4-5 now depend from claim 29.

V. Rejection of Claims as Obvious Over Ramezani *et al.* in view of Deisseroth

The Action next rejects claims 12 and 37 as obvious over the combination of Ramezani *et al.* in view of Deisseroth.

In response, it is noted that, for the reasons discussed above, Ramezani *et al.* is not available as prior art. Thus, the Examiner is requested to reconsider and withdraw this rejection.

VI. Rejection of Claims as Obvious Over Zufferey *et al.* in view of Chang *et al.*

The Action next rejects claims 6-10 and 31 as obvious over Zufferey *et al.* (1998) in view of Chang *et al.*, arguing that Zufferey *et al.* teach transfer vectors having the SIN design but employing only the CMV promoter for transgene expression. The Chang article is cited as demonstrating the use of the EF1α promoter to drive transgene expression in lentivector-transfected hematopoietic progenitor cells. The Action concludes that it would be obvious to replace the CMV promoter to achieve high level expression in hematopoeitic progenitor cells.

In response, Applicants note that claims 6-10 have been amended and now depend from claim 29, which was not rejected over the foregoing combination of references. Furthermore, claim 31 has been cancelled. Thus, the present rejection is now moot.

Nevertheless, it is point out that the Action failed to set forth a *prima facie* obviousness rejection. It is our position that there is no motivation to combine the teachings of Chang *et al.* with those of Zufferey *et al.*, in that there was no reasonable expectation that the SIN design would work in hematopoeitic cells. We have been unable to identify any teaching *per se* in Zufferey *et al.* that would suggest to employ the SIN design in the context of hematopoietic cells, particularly hematopoietic progenitor cells. If the Examiner is aware of any such teaching she is respectfully requested to point it out. In fact, the SIN design incorporates modifications in their LTR region that reduces their promoter activity, and there was simply no way of knowing in advance what effect this would have on its ability to transfect and express in such cells. The reason for this is that neither the transcriptional milieu nor the specificities in hematopoietic

cells, particularly hematopoietic progenitor cells, have been well characterized. As a consequence, the behavior of internal promoters with respect to the LTR regions in the context of a SIN design could not be predicted in advance. Thus, without having a reasonable expectation that a SIN vector could be successfully employed in hematopoietic cells, there would be no reason or basis for modifying the SIN-CMV construct of Zufferey *et al.* Futhermore, Zufferey *et al.* not only fails to suggest the applicability of SIN design vectors to hematopoietic cells, it also appears to be silent as to any drawbacks associated with the CMV promoter in this or any context.

VII. Rejection of Claims as Obvious Over Zufferey *et al.* (1998), in view of Zufferey *et al.* (1999).

The Action next rejects claims 19, 22 and 23 as obvious over the combination of Zufferey *et al.* (1998) in view of Zufferey *et al.* (1999).

Applicants would again note that they are prosecuting the progenitor cell claim, claim 29, for allowance. As this claim was not rejected over this combination, and each of claims 19, 22 and 23 now depend from claim 29, Applicants note that this rejection is now moot.

VIII. Rejection of Claims under 35 U.S.C. §112, First Paragraph

The Action next rejects claims 32-37 under 35 U.S.C. §112, first paragraph, taking the position that the specification is only enabling for *in vitro* transduction of hematopoietic cells and is not enabling for *in vivo* transduction. The Action takes the position that *in vivo* transduction ("gene therapy") has not been demonstrated for hematopoietic progenitor cells.

The claims have been amended such that they read on *in vitro* transduction of the hematopoietic cells. Thus, the "gene therapy" issues raised by the Examiner is now moot. However, Applicants reserve the right to proceed with such subject matter in the context of continuing applications.

IX. Rejection of Claims under 35 U.S.C. §112, Second Paragraph

Lastly, the Action rejects claims 6-10 and 29-37 under 35 U.S.C. §112, second paragraph, for various reasons as discussed below.

First, 6-8 and 31 are rejected due to their use of the phrase "about." The Action contends that "about" means "reasonably close or in the vicinity" and thus is not sufficiently clear when used in the context of defining a signal-to-noise ratio.

Applicants respectfully disagree, and first direct the Examiner's attention to MPEP 2173.05(b) and particularly the section labeled "About". This section, and the cases cited therein, make it clear that the use of the phrase "about" does not render a claim improper under section 112, second paragraph, unless there is close prior art with respect to the particular limitation and that that limitation is critical to distinguishing the invention. Furthermore, it is noted that the term "about" has been interpreted by at least one court in a biotechnology case to mean within the standard error of the measurement technique. See, *e.g.*, *Hybritech Inc. v. Abbott Laboratories*, 4 U.S.P.Q.2d 1001, 1013 (C.D.Cal. 1987), *aff'd*, 849 F.2d 1988 (Fed. Cir. 1988). Applicants respectfully request that the Examiner reconsider and withdraw the rejection as to these claims.

The Action next objects to claim 29, noting that 293T cells are not hematopoietic progenitor cells. Applicants appreciate the Action's noting this typographical error, which has been implicitly addressed herein.

Lastly, with respect to claim 32, the Action takes the position that certain what are said to be "essential steps" are missing. The Action indicates that the claim should be amended to include the specific conditions to effect the transduction of the hematopoietic progenitor cell.

In response, it is first noted that the MPEP section recited by the Action makes it clear that such rejections are appropriate under 35 U.S.C. 112, second paragraph, where "a claim fails to interrelate essential elements." The situation addressed by the Examiner, the inclusion of operable parameters into the claim, has nothing to do with interrelation of elements. Thus,

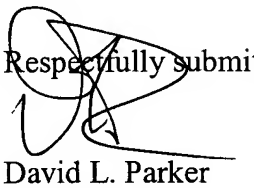
section 112, second paragraph, is not implicated. Further, the Examiner has failed to demonstrate that any such culturing or media conditions are in any way "essential". Lastly, the Examiner's attention is drawn to various decided cases making it clear that section 112, second paragraph, rejections are inappropriate where the basis is the examiner's position that process claims must be amended to recite "operable parameters." See, *e.g.*, *In re Johnson*, 558 F.2d 1008, 194 U.S.P.Q. 187 (CCPA 1977) and *Ex parte Jackson*, 217 U.S.P.Q. 804 (BPAI 1982), both of which stand for the proposition that it is the function of the specification, and not the claims, to set forth operable parameters.

For each of the foregoing reasons, the Examiner is respectfully requested to reconsider and withdraw the section 112, second paragraph, rejection.

X. Conclusion

It is submitted that the present case is now in condition for allowance, and a favorable action is earnestly solicited. In this regard, the Examiner is invited to contact the undersigned attorney at (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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